WEST Search History

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DATE: Tuesday, February 10, 2004

Hide?	Set Name	Query	Hit Count
	DB=USPT,DWPI; PLUR=YES; OP=ADJ		
☐	L1	6344322.pn.	2
	DB=PGPB,USPT,USOC,EPAB,DWPI; PLUR=YES; OP=ADJ		
☐	L2	polyak-K$.in. or vogelstein-B$.in. or kinzler-K$.in.	316
☐	L3	homoplas$ near (mutation or SNP or single basepair or polymorphi$ or variant)	7
☐	L4	l1 and l2	2
☐	L5	l3 and tumor	4

END OF SEARCH HISTORY

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Search Results - Record(s) 1 through 7 of 7 returned.

☐ 1. Document ID: US 20040018538 A1

Using default format because multiple data bases are involved.

L3: Entry 1 of 7 File: PGPB Jan 29, 2004

PGPUB-DOCUMENT-NUMBER: 20040018538
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040018538 A1

TITLE: Mitochondrial dosimeter

PUBLICATION-DATE: January 29, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Fliss, Makiko	Columbia	MD	US	
Sidransky, David	Baltimore	MD	US	
Jen, Jin	Brookville	MD	US	
Polyak, Kornelia	Brookline	MA	US	
Vogelstein, Bert	Baltimore	MD	US	
Kinzler, Kenneth W.	BelAir	MD	US	

US-CL-CURRENT: 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw D

☐ 2. Document ID: US 20030165827 A1

L3: Entry 2 of 7 File: PGPB Sep 4, 2003

PGPUB-DOCUMENT-NUMBER: 20030165827
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030165827 A1

TITLE: Method of detecting mitochondrial dysfunction

PUBLICATION-DATE: September 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Boles, Richard G.	Pasadena	CA	US	

Ito, Masamichi Chestnut Hill MA US

US-CL-CURRENT: 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 3. Document ID: US 20020164622 A1

L3: Entry 3 of 7 File: PGPB Nov 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020164622
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020164622 A1

TITLE: Subtle mitochondrial mutations as tumor markers

PUBLICATION-DATE: November 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Polyak, Kornelia	Brookline	MA	US	
Vogelstein, Bert	Baltimore	MD	US	
Kinzler, Kenneth W.	BelAir	MD	US	

US-CL-CURRENT: 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 4. Document ID: US 6605433 B1

L3: Entry 4 of 7 File: USPT Aug 12, 2003

US-PAT-NO: 6605433
DOCUMENT-IDENTIFIER: US 6605433 B1

TITLE: Mitochondrial dosimeter

DATE-ISSUED: August 12, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fliss; Makiko	Columbia	MD		
Sidransky; David	Baltimore	MD		
Jen; Jin	Brookville	MD		
Polyak; Komelia	Brookline	MA		
Vogelstein; Bert	Baltimore	MD		
Kinzler; Kenneth W.	BelAir	MD		

US-CL-CURRENT: 435/6; 435/91.1, 435/91.2, 436/504, 536/23.1, 536/24.3, 536/24.33

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw D

☐ 5. Document ID: US 6344322 B1

L3: Entry 5 of 7 File: USPT Feb 5, 2002

US-PAT-NO: 6344322
DOCUMENT-IDENTIFIER: US 6344322 B1

TITLE: Subtle mitochondrial mutations as tumor markers

DATE-ISSUED: February 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Polyak; Kornelia	Brookline	MA		
Vogelstein; Bert	Baltimore	MD		
Kinzler; Kenneth W.	BelAir	MD		

US-CL-CURRENT: 435/6; 435/366, 435/91.1, 435/91.2, 536/23.1, 536/24.3, 536/24.33

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw D

☐ 6. Document ID: US 5670320 A

L3: Entry 6 of 7 File: USPT Sep 23, 1997

US-PAT-NO: 5670320
DOCUMENT-IDENTIFIER: US 5670320 A

TITLE: Detection of mitochondrial DNA mutation 14459 associated with dystonia and/or Leber's hereditary optic neuropathy

DATE-ISSUED: September 23, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wallace; Douglas C.	Atlanta	GA		
Brown; Michael D.	Atlanta	GA		

US-CL-CURRENT: 435/6; 435/7.1, 435/7.2, 435/91.2, 536/24.3, 536/24.31, 536/24.32, 536/26.6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw D

☐ 7. Document ID: US 5506101 A

L3: Entry 7 of 7 File: USPT Apr 9, 1996

US-PAT-NO: 5506101
DOCUMENT-IDENTIFIER: US 5506101 A

TITLE: Method for detection of susceptibility mutations for ototoxic deafness

DATE-ISSUED: April 9, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fischel-Ghodsian; Nathan	Los Angeles	CA		
Prezant; Toni R.	Reseda	CA		

US-CL-CURRENT: 435/6; 435/91.2, 536/24.31

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Term	Documents
MUTATION	53013
MUTATIONS	47014
SNP	4062
SNPS	3079
SINGLE	2945584
SINGLES	2866
BASEPAIR	2043
BASEPAIRS	2123
VARIANT	145112
VARIANTS	103585
HOMOPLAS$	0
(HOMOPLAS$ NEAR (MUTATION OR SNP OR SINGLE BASEPAIR OR POLYMORPHI$ OR VARIANT)).PGPB,USPT,USOC,EPAB,DWPI.	7

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http://www.gen.emory.edu/motomap.html. The tend to fall within the D-loop. The effectiveness of therapy can be evaluated when a tumor has already been identified and found to contain a **single basepair** substitution in the mitochondrial genome. Once a **single basepair** mutation has been identified in the mtDNA of a tumor patient, further tumor cells can be detected in tissue surrounding a resection or at other sites, if metastasis has occurred. Similarly, if a tumor has been treated using a non-surgical method such as chemotherapy or radiation, then the success of the therapy can be evaluated at later times by repeating the anal. Specifically, somatic mutations were evaluated in human colorectal tumor cells. Cell fusion expts. have indicated that mitochondria from tumor cells can selectively proliferate when such cells are fused to normal cells. The authors sought to det. whether a similar mitochondrial dominance could be obsd. upon fusion between two colorectal cancer cell lines. These expts. clearly documented that tumor mitochondria of one type can have a significant replicative advantage over other types, and are consistent with other expts. documenting the potential for mitochondrial dominance. Blood, urine, sputum, saliva and feces and other body fluids may all be screened and evaluated for these types of mutation.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 15:24:32 ON 10 FEB 2004)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS' ENTERED AT 15:24:41 ON 10 FEB 2004

L1 2638 S POLYAK K?/AU OR VOGELSTEIN B?/AU OR KINZLER K?/U
L2 2740 S POLYAK K?/AU OR VOGELSTEIN B?/AU OR KINZLER K?/AU
L3 44 S HOMOPLASTIC AND (MUTATION OR SNP OR POLYMORPHIS? OR VARIANT)
L4 0 S TUMOR AND L3
L5 0 S L1 AND L3
L6 1713 S HOMOPLAS? AND (MUTATION OR SNP OR POLYMORPHIS? OR VARIANT)
L7 2 S HOMOPLAS? AND (SINGLE BASEPAIR)
L8 7 S L2 AND L6
L9 80 S L6 AND TUMOR
L10 31 S L9 AND (SUBSTITUTION OR DELETION)
L11 13 DUP REM L10 (18 DUPLICATES REMOVED)

=> dup rem l8
PROCESSING COMPLETED FOR L8
L12 3 DUP REM L8 (4 DUPLICATES REMOVED)

=> d ibib abs l12 1-3

L12 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:192367 BIOSIS
DOCUMENT NUMBER: PREV200200192367
TITLE: Subtle mitochondrial mutations as tumor markers.
AUTHOR(S): **Polyak, Kornelia** [Inventor, Reprint author]; **Vogelstein, Bert** [Inventor]; **Kinzler, Kenneth W.** [Inventor]
CORPORATE SOURCE: Brookline, MA, USA
ASSIGNEE: The Johns Hopkins University
PATENT INFORMATION: US 6344322 February 05, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 5, 2002) Vol. 1255, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

ENTRY DATE: Entered STN: 13 Mar 2002
Last Updated on STN: 13 Mar 2002

AB The accumulation of **homoplasmic** somatic mutations has been observed in the mitochondrial DNA of certain tumor cells. The presence or recurrence of a tumor can be detected by determining the presence of single basepair mutations in the mitochondrial genome from a cell sample of a patient.

L12 ANSWER 2 OF 3 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2000-07385 BIOTECHDS
TITLE: Detecting tumor cells in a patient comprises determining single base pair mutations in the mitochondrial genome of the patient;
method useful for detecting tumor cells
AUTHOR: **Vogelstein B; Kinzler K W; Polyak K**
PATENT ASSIGNEE: Univ.Johns-Hopkins
LOCATION: Baltimore, MD, USA.
PATENT INFO: WO 2000011219 2 Mar 2000
APPLICATION INFO: WO 1999-US18775 20 Aug 1999
PRIORITY INFO: US 1998-97307 20 Aug 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-237667 [20]
AN 2000-07385 BIOTECHDS
AB A method (I) to aid in detecting the presence of tumor cells in a patient sample (blood, urine, feces)is claimed, and comprises determining a single base pair **mutation**(by hybridization of DNA amplified) in a mitochondrial genome of a cell sample from the patient. (I) is used for detecting tumor cells. For example, cellular DNA from VACO cell lines, primary colorectal tumors and normal colonic mucosa were isolated and the mitochondrial genome, was amplified and sequenced. The sequences obtained were compared to those recorded in a mitochondrial data bank, and showed that 3 of the cell lines contained a single **mutation** . While others contained two or three mutations. 12 Mutations were present in the major portion of a mitochondrial DNA molecule and in 10 of the 12 cases the mutations were **homoplasmic**. (29pp)

L12 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999021388 MEDLINE
DOCUMENT NUMBER: 99021388 PubMed ID: 9806551
TITLE: Somatic mutations of the mitochondrial genome in human colorectal tumours.
AUTHOR: **Polyak K**; Li Y; Zhu H; Lengauer C; Willson J K; Markowitz S D; Trush M A; **Kinzler K W**; **Vogelstein B**
CORPORATE SOURCE: The Howard Hughes Medical Institute, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland 21231, USA.
CONTRACT NUMBER: CA 43460 (NCI)
CA 57345 (NCI)
CA 67409 (NCI)
+
SOURCE: NATURE GENETICS, (1998 Nov) 20 (3) 291-3.
Journal code: 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981116
AB Alterations of oxidative phosphorylation in tumour cells were originally

believed to have a causative role in cancerous growth. More recently, mitochondria have again received attention with regards to neoplasia, largely because of their role in apoptosis and other aspects of tumour biology. The mitochondrial genome is particularly susceptible to mutations because of the high level of reactive oxygen species (ROS) generation in this organelle, coupled with a low level of DNA repair. However, no detailed analysis of mitochondrial DNA in human tumours has yet been reported. In this study, we analysed the complete mtDNA genome of ten human colorectal cancer cell lines by sequencing and found mutations in seven (70%). The majority of mutations were transitions at purines, consistent with an ROS-related derivation. The mutations were somatic, and those evaluated occurred in the primary tumour from which the cell line was derived. Most of the mutations were **homoplasmic**, indicating that the mutant genome was dominant at the intracellular and intercellular levels. We showed that mitochondria can rapidly become homogeneous in colorectal cancer cells using cell fusions. These findings provide the first examples of **homoplasmic** mutations in the mtDNA of tumour cells and have potential implications for the abnormal metabolic and apoptotic processes in cancer.

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FILES 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 15:24:41 ON 10 FEB 2004
ALL COPYRIGHTS AND RESTRICTIONS APPLY.  SEE HELP USAGETERMS FOR DETAILS.

7 FILES IN THE FILE LIST

=> POLYAK K?/AU OR VOGELSTEIN B?/AU OR KINZLER k?/u
POLYAK IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s POLYAK K?/AU OR VOGELSTEIN B?/AU OR KINZLER k?/u
'U' IS NOT A VALID FIELD CODE
'U' IS NOT A VALID FIELD CODE
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L1          2638 POLYAK K?/AU OR VOGELSTEIN B?/AU OR KINZLER K?/U

=> s POLYAK K?/AU OR VOGELSTEIN B?/AU OR KINZLER k?/au
L2          2740 POLYAK K?/AU OR VOGELSTEIN B?/AU OR KINZLER K?/AU

=> s homoplastic and (mutation or SNP or polymorphis? or variant)
L3            44 HOMOPLASTIC AND (MUTATION OR SNP OR POLYMORPHIS? OR VARIANT)

=> s tumor and l3
L4             0 TUMOR AND L3

=> s l1 and l3
L5             0 L1 AND L3

=> s homoplas? and (mutation or SNP or polymorphis? or variant)
L6          1713 HOMOPLAS? AND (MUTATION OR SNP OR POLYMORPHIS? OR VARIANT)

=> s homoplas? and (single basepair)
L7             2 HOMOPLAS? AND (SINGLE BASEPAIR)

=> s l2 and l6
L8             7 L2 AND L6

=> s l6 and tumor
L9            80 L6 AND TUMOR

=> s l9 and (substitution or deletion)
L10           31 L9 AND (SUBSTITUTION OR DELETION)

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11           13 DUP REM L10 (18 DUPLICATES REMOVED)

=> d ibib abs l11 1-13

L11  ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:563968  CAPLUS
DOCUMENT NUMBER:          139:346565
TITLE:                    Indels in protein-coding sequences of Euarchontoglires
                          constrain the rooting of the eutherian tree
AUTHOR(S):                de Jong, Wilfried W.; van Dijk, Marjon A. M.; Poux,
                          Celine; Kappe, Guido; van Rheede, Teun; Madsen, Ole
CORPORATE SOURCE:         NCMLS, Department of Biochemistry, University of
                          Nijmegen, Nijmegen, 6500 HB, Neth.
```

SOURCE: Molecular Phylogenetics and Evolution (2003), 28(2), 328-340
CODEN: MPEVEK; ISSN: 1055-7903
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Despite the availability of large mol. data sets, the position of the root of the eutherian tree remains a controversial issue. Depending on source data, taxon sampling and anal. approach, the root can be placed at either Afrotheria, Xenarthra, Afrotheria + Xenarthra, or murid rodents. We explored the phylogenetic potential of indels in four nuclear protein-coding genes (SCA1, PRNP, TNF.alpha., and HspB3) with regard to a possible rooting at the murid branch. According to parsimony principles, five indels were interpreted to contradict such a rooting, and one indel to support it. The results illustrate that indels, despite the occurrence of **homoplasy**, can be convincing sources of independent mol. evidence to distinguish between alternative phylogenetic hypotheses.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:71043 CAPLUS
DOCUMENT NUMBER: 138:366486
TITLE: Mitochondrial DNA damage in non-melanoma skin cancer
AUTHOR(S): Durham, S. E.; Krishnan, K. J.; Betts, J.; Birch-Machin, M. A.
CORPORATE SOURCE: Dept. of Dermatology, School of Clinical and Lab. Sciences, Univ. of Newcastle, Newcastle upon Tyne, NE2 4HH, UK
SOURCE: British Journal of Cancer (2003), 88(1), 90-95
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mitochondrial DNA (mtDNA) damage, predominantly encompassing point mutations, was reported in a variety of cancers. Here the authors present in human skin, the first detailed study of the distribution of multiple forms of mtDNA damage in nonmelanoma skin cancer (NMSC) compared to histol. normal perilesional dermis and epidermis. The authors present the first entire spectrum of deletions found between different types of skin tumors and perilesional skin. In addn., the authors provide the first quant. data for the incidence of the common **deletion** as well as the first report of specific tandem duplications in tumors from any tissue. Importantly, this work shows that there are clear differences in the distribution of deletions between the **tumor** and the histol. normal perilesional skin. Furthermore, DNA sequencing of 4 **mutation** hotspot regions of the mitochondrial genome identified a previously unreported somatic heteroplasmic **mutation** in an SCC patient. In addn., 81 unreported and reported **homoplasmic** single base changes were identified in the other NMSC patients. Unlike the distribution of deletions and the heteroplasmic **mutation**, these **homoplasmic** mutations were present in both **tumor** and perilesional skin, which suggests that for some genetic studies the traditional use of histol. normal perilesional skin from NMSC patients may be limited. Currently, it is unclear whether mtDNA damage has a direct link to skin cancer or it may simply reflect an underlying nuclear DNA instability.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 13 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-08783 BIOTECHDS
TITLE: Detecting the genesis, progression or presence of a disease, e.g. prostate cancer or non melanoma skin cancer by comparing

the mtDNA of a sample to a database containing data of mutations associated with the mitochondrial DNA sequences; DNA-associated **mutation** detection and database comparison for use in disease diagnosis

AUTHOR: BIRCH-MACHIN M; DAKUBO G D; PARR R; THAYER R; NGOM A; TH'NG J
PATENT ASSIGNEE: 1304854 ONTARIO LTD
PATENT INFO: WO 2002101086 19 Dec 2002
APPLICATION INFO: WO 2002-CA848 10 Jun 2002
PRIORITY INFO: US 2001-297340 11 Jun 2001; US 2001-297340 11 Jun 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-148818 [14]
AN 2003-08783 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Detecting (M1) in a subject containing mitochondrial DNA (mtDNA) the genesis or progression, or presence of a disease comprises comparing the mtDNA of the biological sample to a database containing data of mutations associated with the mitochondrial DNA sequences of non-disease and disease associated mitochondrial genomes, is new.

DETAILED DESCRIPTION - (M1) comprises: (a) obtaining a biological sample from the subject; (b) extracting DNA from the biological sample; (c) detecting the presence of mutations in the mtDNA; and (d) comparing the mtDNA of the biological sample to a database containing data of mutations associated with the mitochondrial DNA sequences of non-disease and disease associated mitochondrial genomes. INDEPENDENT CLAIMS are also included for: (1) determining (M2) a predisposition to a disease or disorder indicated by mutations in a mitochondrial DNA sequence; (2) assessing (M3) the status of the aging process of a human subject; (3) a database containing human mitochondrial DNA sequences, such as normal control sequences associated with non-disease states, sequences associated with the presence of disease or sequences indicative of the predisposition to disease; (4) kits for diagnosing, or determining a predisposition to a disease, comprising a disposable chip, a microarray, means for holding the disposable chip, means for extraction of mitochondrial DNA, and means for access to a database of mitochondrial DNA sequences; (5) an array comprising nucleic acid members, and a solid substrate, where each nucleic acid member is indicative of the presence of, or predisposition to a disease, such as mitochondrial DNA or RNA transcribed from mitochondrial DNA, and has a unique position of the array and is stably associated with the solid substrate; (6) diagnosing (M4) a disease, e.g. prostate cancer or non-melanoma skin cancer in a patient by hybridizing a nucleic acid sample obtained from mitochondrial DNA to the array, where the hybridization of the nucleic acid sample to one or more nucleic acid members comprising the array is indicative of the presence of the disease; (7) detecting (M5) heteroplasmy in a subject containing mtDNA; and (8) detecting (M6) mutations associated with disease in a subject containing mtDNA.

BIOTECHNOLOGY - Preferred Method: In detecting in a subject containing mtDNA the genesis or progression, or presence of a disease, the detection of presence of mutations comprises sequencing the mtDNA; amplifying mtDNA by PCR; Southern, Northern, Western and South-Western blot hybridizations; denaturing HPLC; hybridization to microarrays, gene chips or biochips, molecular marker analysis, or any of their combinations. The sequenced mtDNA comprises specific areas of the mitochondrial genome where known biomarkers associated with disease are located, or the entire mitochondrial genome. The biological sample is from a tissue suspected of being a potential site of a disease, or suspected of harboring a metastasis. The disease is prostate cancer or non-melanoma skin cancer. The **mutation** can be single base pair mutations, deletions, insertions or transversions. This **mutation** can either be **homoplasmic**, or heteroplasmic at any level. The biological sample is blood, sputum, buccal cells, saliva, prostate massage fluid, sweat, cervical tissue from a PAP smear, urine, skin cells, bone, hair, lymph tissue, cervical smears, breast aspirate, fecal

matter, ejaculate, menstrual flow or biopsy tissue Determining a predisposition to a disease or disorder indicated by mutations in a mitochondrial DNA sequence, and assessing the status of the aging process of a human subject comprise the steps cited for detecting in a subject containing mtDNA the genesis or progression, or presence of a disease. Diagnosing a disease further comprises isolating a prostate massage fluid sample or a skin sample from the patient, and preparing a nucleic acid sample from the prostate massage fluid sample or a skin sample. Detecting heteroplasmy in a subject containing mtDNA comprises obtaining a biological sample from the subject, extracting DNA from the biological sample, and performing denaturing HPLC on the sample. Detecting mutations associated with disease in a subject comprises obtaining a biological sample from the subject, extracting DNA from the biological sample, detecting the presence of mutations in the mtDNA, and comparing the mtDNA of the biological sample to a database containing data of common population variants in non-disease and disease associated mitochondrial genomes. Preferred Database: The database contains at least a statistically significant number of mitochondrial DNA sequences having been obtained from the maternal line and non-maternal line samples. The mitochondrial DNA sequences are associated with the aging process of a human subject.

USE - (M1) is useful for diagnosing diseases, such as prostate cancer or non-melanoma skin cancer (claimed).

EXAMPLE - To simultaneously detect and quantify the ratios of both deleted and wild type mtDNAs in the DNA samples, a 3-primer PCR procedure was used. Primers A and C correspond to heavy strand positions 13720-13705 and 9028-9008 respectively. Primer B corresponds to light strand positions 8273-8289. Primer C maps to a mtDNA region within the common **deletion**, whereas primers A and B flank the deleted region. Therefore, primers B and C amplify wt-mtDNAs and primers A and B amplify deleted mtDNAs.(67 pages)

L11 ANSWER 4 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2002717790 MEDLINE
DOCUMENT NUMBER: 22367642 PubMed ID: 12479093
TITLE: Mitochondrial DNA mutations in lung cancer.
AUTHOR: Jin Xiong-jie; Zhang Jian-jun; Song Yan; Gao Yan-ning; Cheng Shu-jun
CORPORATE SOURCE: Cancer Institute (Hospital), Chinese Academy of Medical Sciences & Peking Union Medical College, Chinese Human Genome Center, Beijing, P. R. China.
SOURCE: Ai Zheng, (2002 Jul) 21 (7) 715-8.
Journal code: 9424852. ISSN: 1000-467X.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021218
Last Updated on STN: 20021231
Entered Medline: 20021230

AB BACKGROUND AND OBJECTIVE: Mitochondiral DNA (mtDNA) mutations has been identified in various cancers, but their significance was unknown. This study aimed to detect mtDNA mutations in lung cancer, and to investigate their roles in the carcinogenesis of human lung. METHODS: Total DNA (including nuclear DNA and mtDNA) was extracted from the **tumor** tissues, corresponding distal non-cancerous lung tissues, and peripheral lymphocytes derived from 58 patients with lung cancer. Fifty-eight overlapping fragments and covering complete sequence of mtDNA were amplified by nested PCR, and the PCR products were sequenced directly with the cycle sequencing methods. The mtDNA mutations in the **tumor** tissue were determined by comparing with corresponding and peripheral lymphocytes. RESULTS: Sixty-six mutations were identified in 36 cases (62.1%) of lung cancer, including 58 point mutations, 4 insertions, and 4

deletions. These mutations were dispersedly distributed in the full length of mtDNA. The frequency of **mutation** in D-loop is the highest, in which 18 mutations were detected. No **mutation** hot spot was found in peptide-coding regions. Among 43 point mutations identified in protein-coding region, 20 were silent mutations. In 8 patients, identical mutations were detected both in the **tumor** tissues and corresponding distal non-cancerous tissues. CONCLUSION: Most of mtDNA mutations in the lung cancers investigated were occurred randomly and might have no impact on carcinogenesis; whereas the **homoplasmic** mutations may provide a potential diagnostic marker for lung cancer.

L11 ANSWER 5 OF 13 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001547925 MEDLINE
DOCUMENT NUMBER: 21469637 PubMed ID: 11585726
TITLE: Identification of a mononucleotide repeat as a major target for mitochondrial DNA alterations in human tumors.
AUTHOR: Sanchez-Cespedes M; Parrella P; Nomoto S; Cohen D; Xiao Y; Esteller M; Jeronimo C; Jordan R C; Nicol T; Koch W M; Schoenberg M; Mazzarelli P; Fazio V M; Sidransky D
CORPORATE SOURCE: Department of Otolaryngology-Head and Neck Surgery, Head and Neck Cancer Research Division, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205-2196, USA.
CONTRACT NUMBER: CA-58184-03 (NCI)
UO1-CA-98-028 (NCI)
SOURCE: CANCER RESEARCH, (2001 Oct 1) 61 (19) 7015-9.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011015
Last Updated on STN: 20011022
Entered Medline: 20011018

AB Mitochondrial DNA (mtDNA) mutations scattered through coding and noncoding regions have been reported in cancer. The mechanisms that generate such mutations and the importance of mtDNA mutations in **tumor** development are still not clear. Here we present the identification of a specific and highly polymorphic homopolymeric C stretch (D310), located within the displacement (D) loop, as a mutational hotspot in primary tumors. Twenty-two % of the 247 primary tumors analyzed harbored somatic deletions/insertions at this mononucleotide repeat. Moreover, these alterations were also present in head and neck preneoplastic lesions. We further characterized the D310 variants that appeared in the lung and head and neck tumors. Most of the somatic alterations found in tumors showed **deletion**/insertions of 1- or 2-bp generating D310 variants identical to constitutive **polymorphisms** described previously. Sequencing analysis of individual clones from lymphocytes revealed that patients with D310 mutations in the tumors had statistically significant higher levels of D310 heteroplasmy (more than one length **variant**) in the lymphocyte mtDNA as compared with the patients without D310 mutations in the **tumor** mtDNA. On the basis of our observations, we propose a model in which D310 alterations are already present in normal cells and achieve **homoplasmy** in the **tumor** through a restriction/amplification event attributable to random genetic drift and clonal expansion.

L11 ANSWER 6 OF 13 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 2
ACCESSION NUMBER: 2001294258 EMBASE
TITLE: High incidence of somatic mitochondrial DNA mutations in human ovarian carcinomas.
AUTHOR: Liu V.W.S.; Hong Hui Shi; Cheung A.N.Y.; Pui Man Chiu; Tsin

Wah Leung; Nagley P.; Ling Wong Wong; Ngan H.Y.S.
CORPORATE SOURCE: H.Y.S. Ngan, Department of Obstetrics, University of Hong Kong, Queen Mary Hospital, Pokfulam Road, Hong Kong, Hong Kong. hysngan@hkucc.hku.hk
SOURCE: Cancer Research, (15 Aug 2001) 61/16 (5998-6001).
Refs: 20
ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English

AB To investigate the potential role of somatic mitochondrial DNA (mtDNA) mutations in tumorigenesis, the occurrence of mutations in mtDNA of ovarian carcinomas was studied. We sequenced the D-loop region of mtDNA of 15 primary ovarian carcinomas and their matched normal controls. Somatic mtDNA mutations were detected in 20% (3 of 15) **tumor** samples carrying single or multiple changes. Complete sequence analysis of the mtDNA genomes of another 10 pairs of primary ovarian carcinomas and control tissues revealed somatic mtDNA mutations in 60% (6 of 10) of **tumor** samples. Most of these mutations were **homoplasmic**, and most were T.fwdarw.C or G.fwdarw.A transitions, but one represented a differential length within a run of identical C residues. A region of mtDNA sequence including the 16S and 12S rRNA genes, the D-loop and the cytochrome b gene, may represent the zone of preferred mtDNA **mutation** in ovarian cancer. The high incidence of mtDNA mutations found in ovarian carcinomas and other human cancers suggests that genetic instability of mtDNA might play a significant role in tumori-genesis.

ACCESSION NUMBER: 2001268982 EMBASE
TITLE: High frequency of mitochondrial DNA mutations in glioblastoma multiforme identified by direct sequence comparison to blood samples.
AUTHOR: Kirsches E.; Krause G.; Warich-Kirches M.; Weis S.; Scheineder T.; Meyer-Puttlitz B.; Mawrin C.; Dietzmann K.
CORPORATE SOURCE: E. Kirsches, Institute of Neuropathology, University of Magdeburg, Leipziger Str. 44, 39120 Magdeburg, Germany. elmar.kirches@medizin.uni-magdeburgde
SOURCE: International Journal of Cancer, (15 Aug 2001) 93/4 (534-538).
Refs: 33
ISSN: 0020-7136 CODEN: IJCNAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In an earlier study, we showed that heteroplasmy in the mitochondrial genome of gliomas sometimes occurs in a D-loop polycytosine tract. We extended this study by pairwise comparisons between glioma samples and adjacent brain tissue of 55 patients (50 glioblastomas, I astrocytoma WHO grade III, 4 astrocytomas WHO grade II). We used a combination of laser microdissection and PCR to detect and quantify variations in the polycytosine tract. New length variants undetectable in the adjacent brain tissue were observed in 5 glioblastomas (9%). In 2 of these cases, samples from a lower **tumor** stage (WHO grade II) could be analyzed and revealed the early occurrence of these mutations in both cases. Since the mitochondrial D-loop contains additional repeats and highly polymorphic non-coding sequences, we compared 17 glioblastomas with the corresponding blood samples of the same patients by direct sequencing of the complete D-loop. In 6 of these tumors (35%), instability was detected in 1 or 2 of 3 repeat regions; in I of these repeats, the instability was linked to a

germline T-to-C transition. Furthermore, of 2 tumors (12%) 1 carried 1 and the other 9 additional transitions. In the latter patient, 6.7 kb of the protein coding mtDNA sequence were analyzed. Six silent transitions and 2 missense mutations (transitions) were found. All base substitutions appeared to be **homoplasmic** upon sequencing, and 89% occurred at known polymorphic sites in humans. Our data suggest that the same mechanisms that generate inherited mtDNA **polymorphisms** are strongly enhanced in gliomas and produce somatic mutations. .COPYRGT. 2001 Wiley-Liss, Inc.

L11 ANSWER 8 OF 13 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 4

ACCESSION NUMBER: 2001075060 EMBASE
TITLE: Mitochondrial genome instability in human cancers.
AUTHOR: Bianchi N.O.; Bianchi M.S.; Richard S.M.
CORPORATE SOURCE: N.O. Bianchi, Inst. Multidisciplinario Biol. Cel., CC 403, 1900 La Plata, Argentina. bianchi@satlink.com
SOURCE: Mutation Research - Reviews in Mutation Research, (2001) 488/1 (9-23).
Refs: 108
ISSN: 1383-5742 CODEN: MRRRFK
PUBLISHER IDENT.: S 1383-5742(00)00063-6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Malfunction of mismatch repair (MMR) genes produces nuclear genome instability (NGI) and plays an important role in the origin of some hereditary and sporadic human cancers. The appearance of non-inherited microsatellite alleles in **tumor** cells (microsatellite instability, MSI) is one of the expressions of NGI. We present here data showing mitochondrial genome instability (mtGI) in most of the human cancers analyzed so far. The mtDNA markers used were point mutations, length-tract instability of mono- or dinucleotide repeats, mono- or dinucleotide insertions or deletions, and long deletions. Comparison of normal and tumoral tissues from the same individual reveals that mt-mutations may show as **homoplasmic** (all **tumor** cells have the same **variant** haplotype) or as heteroplasmic (**tumor** cells are a mosaic of inherited and acquired **variant** haplotypes). Breast, colorectal, gastric and kidney cancers exhibit mtGI with a pattern of mt-mutations specific for each **tumor**. No correlation between NGI and mtGI was found in breast, colorectal or kidney cancers, while a positive correlation was found in gastric cancer. Conversely, germ cell testicular cancers lack mtGI. Damage by reactive oxygen species (ROS), slipped-strand mispairing (SSM) and deficient repair are the causes explaining the appearance of mtGI. The replication and repair of mtDNA are controlled by nuclear genes. So far, there is no clear evidence linking MMR gene malfunction with mtGI. Polymerase .gamma. (POL.gamma.) carries out the mtDNA synthesis. Since this process is error-prone due to a deficiency in the proofreading activity of POL.gamma., this enzyme has been assumed to be involved in the origin of mt-mutations. Somatic cells have hundreds to thousands of mtDNA molecules with a very high rate of spontaneous mutations. Accordingly, most somatic cells probably have a low frequency of randomly mutated mtDNA molecules. Most cancers are of monoclonal origin. Hence, to explain the appearance of mtGI in tumors we have to explain why a given **variant** mt-haplotype expands and replaces part of (heteroplasmy) or all (**homoplasmy**) wild mt-haplotypes in cancer cells. Selective and/or replicative advantage of some mutations combined with a severe bottleneck during the mitochondrial segregation accompanying mitosis are the mechanisms probably involved in the origin of mtGI. .COPYRGT. 2001 Elsevier Science B.V.

L11 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:145068 CAPLUS
DOCUMENT NUMBER: 132:176590
TITLE: methods to detect subtle mitochondrial mutations as **tumor** markers with specific examples relating to colorectal cancer
INVENTOR(S): Vogelstein, Bert; Kinzler, Kenneth W.; Polyak, Kornelia
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000011219	A1	20000302	WO 1999-US18775	19990820
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2340175	AA	20000302	CA 1999-2340175	19990820
AU 9956778	A1	20000314	AU 1999-56778	19990820
EP 1104492	A1	20010606	EP 1999-943742	19990820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002523061	T2	20020730	JP 2000-566470	19990820
NO 2001000843	A	20010418	NO 2001-843	20010219

PRIORITY APPLN. INFO.:		
US 1998-97307P	P	19980820
WO 1999-US18775	W	19990820

AB The accumulation of **homoplasmic** somatic mutations has been obsd. in the mitochondrial DNA of certain **tumor** cells and/or cancer. This **mutation** may be a **substitution**, insertion, **deletion**, or transition. The presence or a recurrence of a **tumor** can be detected by detg. the presence of single basepair mutations in the mitochondrial genome from a cell sample of a patient. This paper describes new methods for detecting and tracing tumors by examg. mtDNA for appearance of somatic mutations. These were traced using the NlaIII restriction endonuclease to monitor creation/destruction of this restriction site by the **mutation**. Mutations, however can first be identified by comparison to sequences present in public databases for human mitochondrial DNA, e.g. at http://www.gen.emory.edu/motomap.html . The tend to fall within the D-loop. The effectiveness of therapy can be evaluated when a **tumor** has already been identified and found to contain a single basepair **substitution** in the mitochondrial genome. Once a single basepair **mutation** has been identified in the mtDNA of a **tumor** patient, further **tumor** cells can be detected in tissue surrounding a resection or at other sites, if metastasis has occurred. Similarly, if a **tumor** has been treated using a non-surgical method such as chemotherapy or radiation, then the success of the therapy can be evaluated at later times by repeating the anal. Specifically, somatic mutations were evaluated in human colorectal **tumor** cells. Cell fusion expts. have indicated that mitochondria from **tumor** cells can selectively proliferate when such cells are fused to normal cells. The authors sought to det. whether a similar mitochondrial dominance could be obsd. upon fusion between two colorectal

cancer cell lines. These expts. clearly documented that **tumor** mitochondria of one type can have a significant replicative advantage over other types, and are consistent with other expts. documenting the potential for mitochondrial dominance. Blood, urine, sputum, saliva and feces and other body fluids may all be screened and evaluated for these types of **mutation**.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 13 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2000250969 MEDLINE
DOCUMENT NUMBER: 20250969 PubMed ID: 10788526
TITLE: A pathogenic 15-base pair **deletion** in mitochondrial DNA-encoded cytochrome c oxidase subunit III results in the absence of functional cytochrome c oxidase.
AUTHOR: Hoffbuhr K C; Davidson E; Filiano B A; Davidson M; Kennaway N G; King M P
CORPORATE SOURCE: Department of Molecular and Medical Genetics, Oregon Health Sciences University, Portland, Oregon 97201, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 May 5) 275 (18) 13994-4003.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000613
Last Updated on STN: 20000613
Entered Medline: 20000601

AB A 15-base pair, in-frame, **deletion** (9480del15) in the mitochondrial DNA (mtDNA)-encoded cytochrome c oxidase subunit III (COX III) gene was identified previously in a patient with recurrent episodes of myoglobinuria and an isolated COX deficiency. Transmitochondrial cell lines harboring 0, 97, and 100% of the 9480del15 **deletion** were created by fusing human cells lacking mtDNA (rho(0) cells) with platelet and lymphocyte fractions isolated from the patient. The COX III gene **mutation** resulted in a severe respiratory chain defect in all mutant cell lines. Cells **homoplasmic** for the **mutation** had no detectable COX activity or respiratory ATP synthesis, and required uridine and pyruvate supplementation for growth, a phenotype similar to rho(0) cells. The cells with 97% mutated mtDNA exhibited severe reductions in both COX activity (6% of wild-type levels) and rates of ATP synthesis (9% of wild-type). The COX III polypeptide in the mutant cells, although translated at rates similar to wild-type, had reduced stability. There was no evidence for assembly of COX I, COX II, or COX III subunits in a multisubunit complex in cells **homoplasmic** for the **mutation**, thus indicating that there was no stable assembly of COX I with COX II in the absence of wild-type COX III. In contrast, the COX I and COX II subunits were assembled in cells with 97% mutated mtDNA.

L11 ANSWER 11 OF 13 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2000185707 MEDLINE
DOCUMENT NUMBER: 20185707 PubMed ID: 10720328
TITLE: Facile detection of mitochondrial DNA mutations in tumors and bodily fluids.
AUTHOR: Fliss M S; Usadel H; Caballero O L; Wu L; Buta M R; Eleff S M; Jen J; Sidransky D
CORPORATE SOURCE: Department of Otolaryngology-Head and Neck Surgery, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.
CONTRACT NUMBER: PO1 CA 58184 (NCI)
RO1 CA77664 (NCI)
RO1 DE 012488 (NIDCR)

+
SOURCE: SCIENCE, (2000 Mar 17) 287 (5460) 2017-9.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000413
Last Updated on STN: 20000413
Entered Medline: 20000404

AB Examination of human bladder, head and neck, and lung primary tumors revealed a high frequency of mitochondrial DNA (mtDNA) mutations. The majority of these somatic mutations were **homoplasmic** in nature, indicating that the mutant mtDNA became dominant in **tumor** cells. The mutated mtDNA was readily detectable in paired bodily fluids from each type of cancer and was 19 to 220 times as abundant as mutated nuclear p53 DNA. By virtue of their clonal nature and high copy number, mitochondrial mutations may provide a powerful molecular marker for noninvasive detection of cancer.

L11 ANSWER 12 OF 13 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000438456 MEDLINE
DOCUMENT NUMBER: 20407452 PubMed ID: 10948273
TITLE: Evolution of microsatellite alleles in four species of mice (genus Apodemus).
AUTHOR: Makova K D; Nekrutenko A; Baker R J
CORPORATE SOURCE: Department of Biological Sciences, Texas Tech University, Lubbock, TX 79409 USA.. kmakova@midway.uchicago.edu
SOURCE: JOURNAL OF MOLECULAR EVOLUTION, (2000 Aug) 51 (2) 166-72.
Journal code: 0360051. ISSN: 0022-2844.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
OTHER SOURCE: GENBANK-AF127351; GENBANK-AF127352; GENBANK-AF127353; GENBANK-AF127354; GENBANK-AF127355; GENBANK-AF127356; GENBANK-AF127357; GENBANK-AF127358; GENBANK-AF127359; GENBANK-AF127360; GENBANK-AF127361; GENBANK-AF127362; GENBANK-AF127363; GENBANK-AF127364; GENBANK-AF127365; GENBANK-AF127366; GENBANK-AF127367; GENBANK-AF127368; GENBANK-AF127369; GENBANK-AF127370; GENBANK-AF127535; GENBANK-AF127536; GENBANK-AF127537; GENBANK-AF127538; GENBANK-AF127539; GENBANK-AF127540; GENBANK-AF127541; GENBANK-AF127542; GENBANK-AF127543
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000919

AB Microsatellite length variation was investigated at a highly variable microsatellite locus in four species of Apodemus. Information obtained from microsatellite allele sequences was contrasted with allele sizes, which included 18 electromorphs. Additional analysis of a 400-bp unique sequence in the flanking region identified 26 different haplotype sequences or "true" alleles in the sample. Three molecular mechanisms, namely, (1) addition/**deletion** of repeats, (2) substitutions and indels in the flanking region, and (3) mutations interrupting the repeat, contributed to the generation of allelic variation. Size **homoplasy** can be inferred for alleles within populations, from different populations of the same species, and from different species. We propose that microsatellite flanking sequences may be informative markers for investigating **mutation** processes in microsatellite repeats as well as phylogenetic relationships among alleles, populations, and species.

L11 ANSWER 13 OF 13 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 96010274 MEDLINE
DOCUMENT NUMBER: 96010274 PubMed ID: 7573355
TITLE: Somatic mitochondrial **mutation** in gastric cancer.
AUTHOR: Burgart L J; Zheng J; Shu Q; Strickler J G; Shibata D
CORPORATE SOURCE: Department of Anatomic Pathology, Mayo Clinic, Rochester, Minnesota, USA.
CONTRACT NUMBER: CA-58704 (NCI)
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (1995 Oct) 147 (4) 1105-11. Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19951227
Entered Medline: 19951109

AB Likely hot spots for mutations are mitochondrial sequences as there is less repair and more damage by carcinogens compared with nuclear sequences. A somatic 50-bp mitochondrial D-loop **deletion** was detected in four gastric adenocarcinomas. The **deletion** included the CSB2 region and was flanked by 9-bp direct repeats. The **deletion** was more frequent in adenocarcinomas arising from the gastroesophageal junction (4/32, 12.5%) compared with more distal tumors (0/45). Topographical analysis revealed the absence of the **deletion** from normal tissues except in focal portions of smooth muscle in one case. In two cases, apparent mutant **homoplasmy** was present throughout two tumors, including their metastases. In the two other cases, the **mutation** was present in only minor focal portions (< 5%) of their primary tumors. These findings document the presence of somatic mitochondrial alterations in gastric cancer, which may reflect the environmental and genetic influences operative during **tumor** progression.

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(FILE 'HOME' ENTERED AT 15:24:32 ON 10 FEB 2004)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 15:24:41 ON 10 FEB 2004

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L1          2638 S POLYAK K?/AU OR VOGELSTEIN B?/AU OR KINZLER K?/U
L2          2740 S POLYAK K?/AU OR VOGELSTEIN B?/AU OR KINZLER K?/AU
L3            44 S HOMOPLASTIC AND (MUTATION OR SNP OR POLYMORPHIS? OR VARIANT)
L4             0 S TUMOR AND L3
L5             0 S L1 AND L3
L6          1713 S HOMOPLAS? AND (MUTATION OR SNP OR POLYMORPHIS? OR VARIANT)
L7             2 S HOMOPLAS? AND (SINGLE BASEPAIR)
L8             7 S L2 AND L6
L9            80 S L6 AND TUMOR
L10           31 S L9 AND (SUBSTITUTION OR DELETION)
L11           13 DUP REM L10 (18 DUPLICATES REMOVED)
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=> d ibib abs l7 1-2

L7 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:192367 BIOSIS
DOCUMENT NUMBER: PREV200200192367
TITLE: Subtle mitochondrial mutations as tumor markers.
AUTHOR(S): Polyak, Kornelia [Inventor, Reprint author]; Vogelstein, Bert [Inventor]; Kinzler, Kenneth W. [Inventor]
CORPORATE SOURCE: Brookline, MA, USA

ASSIGNEE: The Johns Hopkins University
PATENT INFORMATION: US 6344322 February 05, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 5, 2002) Vol. 1255, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Mar 2002
Last Updated on STN: 13 Mar 2002

AB The accumulation of **homoplasmic** somatic mutations has been observed in the mitochondrial DNA of certain tumor cells. The presence or recurrence of a tumor can be detected by determining the presence of **single basepair** mutations in the mitochondrial genome from a cell sample of a patient.

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:145068 CAPLUS
DOCUMENT NUMBER: 132:176590
TITLE: methods to detect subtle mitochondrial mutations as tumor markers with specific examples relating to colorectal cancer
INVENTOR(S): Vogelstein, Bert; Kinzler, Kenneth W.; Polyak, Kornelia
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000011219	A1	20000302	WO 1999-US18775	19990820
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2340175	AA	20000302	CA 1999-2340175	19990820
AU 9956778	A1	20000314	AU 1999-56778	19990820
EP 1104492	A1	20010606	EP 1999-943742	19990820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002523061	T2	20020730	JP 2000-566470	19990820
NO 2001000843	A	20010418	NO 2001-843	20010219

PRIORITY APPLN. INFO.: US 1998-97307P P 19980820
WO 1999-US18775 W 19990820

AB The accumulation of **homoplasmic** somatic mutations has been obsd. in the mitochondrial DNA of certain tumor cells and/or cancer. This mutation may be a substitution, insertion, deletion, or transition. The presence or a recurrence of a tumor can be detected by detg. the presence of **single basepair** mutations in the mitochondrial genome from a cell sample of a patient. This paper describes new methods for detecting and tracing tumors by examg. mtDNA for appearance of somatic mutations. These were traced using the NlaIII restriction endonuclease to monitor creation/destruction of this restriction site by the mutation. Mutations, however can first be identified by comparison to sequences present in public databases for human mitochondrial DNA, e.g. at

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
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 NEWS  8  OCT 28   BIOSIS file segment of TOXCENTER reloaded and enhanced
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 NEWS 11  DEC 08   IMS file names changed
 NEWS 12  DEC 09   Experimental property data collected by CAS now available
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 NEWS 13  DEC 09   STN Entry Date available for display in REGISTRY and CA/CAplus
 NEWS 14  DEC 17   DGENE: Two new display fields added
 NEWS 15  DEC 18   BIOTECHNO no longer updated
 NEWS 16  DEC 19   CROPU no longer updated; subscriber discount no longer
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 NEWS 17  DEC 22   Additional INPI reactions and pre-1907 documents added to CAS
                   databases
 NEWS 18  DEC 22   IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
 NEWS 19  DEC 22   ABI-INFORM now available on STN
 NEWS 20  JAN 27   Source of Registration (SR) information in REGISTRY updated
                   and searchable
 NEWS 21  JAN 27   A new search aid, the Company Name Thesaurus, available in
                   CA/CAplus
 NEWS 22  FEB 05   German (DE) application and patent publication number format
                   changes

 NEWS EXPRESS  DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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    FILE .BIOTECH CAPLUS
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                                                          ENTRY    SESSION
      ESTIMATED COST                                       0.21       0.21
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